

**WHAT IS CLAIMED IS:**

1. An isolated and purified nucleic acid segment comprising a nucleic acid sequence comprising a desosamine biosynthetic gene cluster, a fragment or a biologically active variant thereof, wherein the nucleic acid sequence is not derived from the *eryC* gene cluster of *Saccharopolyspora erythraea* or *Streptomyces antibioticus*.
2. The isolated and purified nucleic acid segment of claim 1 comprising SEQ ID NO:3.
3. The isolated and purified nucleic acid segment of claim 1 which encodes DesI, DesII, DesIII, DesIV, DesV, DesVI, DesVII, DesVIII or DesR.
4. The isolated and purified nucleic acid segment of any one of claims 1 to 3 which is from *Streptomyces venezuelae*.
5. An expression cassette comprising the nucleic acid segment of any one of claims 1 to 4 operably linked to a promoter functional in a host cell.
6. A recombinant bacterial host cell in which at least a portion of a nucleic acid sequence encoding desosamine is disrupted so as to alter desosamine synthesis, wherein the nucleic acid sequence which is disrupted is not derived from the *eryC* gene cluster of *Saccharopolyspora erythraea*.
7. The host cell of claim 6 wherein the nucleic acid sequence which is disrupted encodes DesI, DesII, DesIII, DesIV, DesV, DesVI, DesVII, DesVIII or DesR.
8. A host cell, the genome of which is augmented with the expression cassette of claim 5.
9. A product produced by the host cell of any one of claims 6 to 8 which is not produced by the corresponding non-recombinant or non-augmented host cell.
10. The product of claim 9 which comprises a macrolide.

T06T1-1888650

11. The product of claim 9 or 10 which is biologically active.
12. An isolated and purified nucleic acid segment comprising a nucleic acid sequence comprising a macrolide biosynthetic gene cluster encoding polypeptides which synthesize methymycin, pikromycin, neomethymycin, narbomycin, or a combination thereof, or a biologically active variant or fragment thereof.
13. The isolated and purified nucleic acid segment of claim 12 comprising SEQ ID NO:5.
14. The isolated and purified nucleic acid segment of claim 12 comprising a biologically active variant or fragment of SEQ ID NO:5.
15. The isolated and purified nucleic acid segment of claim 12 which encodes PikR1, PikR2, PikAI, PikAII, PikAIII, PikAIV, PikAV, PikC or PikD.
16. The isolated and purified nucleic acid segment of any one of claims 12 to 15 which is from *Streptomyces venezuelae*.
17. A host cell, the genome of which is augmented with the nucleic acid segment of any one of claims 12 to 16.
18. An isolated and purified nucleic acid sequence comprising SEQ ID NO:3, SEQ ID NO:5, a fragment thereof, the complement thereto, or which hybridizes thereto.
19. An isolated polypeptide encoded by the nucleic acid segment of any one of claims 1 to 4 or 12 to 16.
20. A recombinant host cell in which a *pikAI* gene, a *pikAII* gene, a *pikAIII* gene, a *pikAIV* gene, a *pikB* gene cluster, a *pikAV* gene cluster, a *pikC* gene, a *pikR1* gene, a *pikR2* gene, or a combination thereof, is disrupted so as to alter production of methymycin, neomethymycin, pikromycin, narbomycin, or a combination thereof.

21. A macrolide or polyketide product produced by the host cell of claim 17 or 20 which is not produced by the corresponding non-recombinant or non-augmented host cell.
22. The macrolide or polyketide of claim 21 which is biologically active.
23. An isolated and purified DNA molecule comprising a first DNA segment encoding a first module and a second DNA segment encoding a second module, wherein the DNA segments together encode a recombinant polyhydroxyalkanoate monomer synthase, and wherein at least one DNA segment is derived from the *pikA* gene cluster of *Streptomyces venezuelae*.
24. A method of providing a polyhydroxyalkanoate monomer, comprising:
  - (a) introducing into a host cell a DNA molecule comprising a DNA segment encoding a recombinant polyhydroxyalkanoate monomer synthase operably linked to a promoter functional in the host cell, wherein the recombinant polyhydroxyalkanoate monomer synthase comprises a first module and a second module, and wherein at least one DNA segment is derived from the *pikA* gene cluster of *Streptomyces venezuelae*; and
  - (b) expressing the DNA encoding the recombinant polyhydroxyalkanoate monomer synthase in the host cell so as to generate a polyhydroxyalkanoate monomer.
25. A recombinant vector comprising one or more modules of a polyketide synthase wherein at least one module is from *Streptomyces venezuelae*.
26. The method of claim 24 wherein the first module encodes a fatty acid synthase.
27. A method of providing a polyhydroxyalkanoate monomer, comprising:
  - (a) introducing into a host cell a DNA molecule encoding a fusion polypeptide, wherein the DNA molecule comprises a first DNA segment operably linked to a promoter functional in the host cell and a second DNA segment, wherein at least one DNA segment is derived from the *pikA* gene cluster of *Streptomyces venezuelae*; and

T:0677"4888660

- (b) expressing the DNA in the host cell so as to generate the fusion polypeptide.
28. The host cell of claim 8 or 17 the native genome of which does not comprise an intact macrolide biosynthetic gene cluster encoding polypeptides which synthesize methymycin, pikromycin, neomethymycin, or narbomycin.
29. A recombinant bacterial host cell comprising a deletion of the thioesterase domain of *pikAIV* gene.
30. The recombinant host cell of claim 29 further comprising a deletion in the *pikAV* gene.
31. An isolated and purified DNA molecule comprising a DNA segment comprising a *pikA* promoter.
32. An expression cassette comprising a *pikA* promoter operably linked to a DNA molecule comprising a DNA segment comprising an open reading frame or a portion thereof.
33. The expression cassette of claim 32 wherein the DNA segment encodes the thioesterase domain of *pikAIV*.
34. The expression cassette of claim 32 wherein the DNA segment encodes the thioesterase II domain of *pikAV*.
35. The expression cassette of claim 33 further comprising an acyl carrier protein domain.
36. The expression cassette of claim 35 further comprising a thioesterase II domain.
37. The expression cassette of claim 35 further comprising an acyl transferase domain.
38. The expression cassette of claim 37 further comprising a  $\beta$ -ketoacyl-acyl carrier protein synthase domain.

09988384-11901  
FOOTNOTES

39. The expression cassette of any one of claims 32 to 38 wherein the DNA molecule comprises a second DNA segment comprising the leader sequence of *pikAI* operably linked to the first DNA segment.
40. A host cell transformed with a plasmid comprising the expression cassette of any one of claims 32 to 39.
41. The host cell of claim 40 which lacks the thioesterase domain of *pikAIV* gene cluster and the thioesterase II domain of *pikAV* gene.
42. A method to alter polyketide chain length, comprising: expressing in a host cell an expression cassette comprising at least a portion of a DNA segment that encodes a module that catalyzes the final condensation of a polyketide so as to yield a polyketide product which is of a different length relative to a polyketide produced by a host cell which does not express the module, wherein the DNA segment that encodes an intact module encodes two different polypeptides, one of which has a lower molecular weight than the other polypeptide.
43. The method of claim 42 wherein the intact module is *pikA* module 6.
44. The method of claim 42 wherein the expression cassette is present on a plasmid.
45. The method of claim 42 wherein the host cell is a polyketide-producing host cell.
46. A product produced by the method of claim 42 which is not produced by a host cell which does not express the module.
47. A method to prepare a polyketide product, comprising: expressing in a host cell an expression cassette comprising a promoter operably linked to a DNA segment comprising a portion of a first polyketide synthase gene so as to yield the product, wherein the expression cassette is present on a plasmid, wherein the chromosome of the host cell comprises at least a portion of a second polyketide synthase gene, and

wherein both portions are operably linked to the native polyketide promoter of one of the polyketide genes.

48. The method of claim 47 wherein the portions are from the same polyketide gene and wherein the portion on the host cell chromosome is different than the portion that is on the plasmid.
49. The method of claim 48 wherein the portions together comprise the entire gene.
50. The method of claim 49 wherein the gene is the *pikA* gene cluster.
51. A host cell, the genome of which comprises at least a portion of a first polyketide synthase gene, comprising: a plasmid comprising a promoter operably linked to a DNA molecule comprising a DNA segment encoding a portion of a second polyketide synthase gene, wherein both portions are operably linked to the native promoter of one of the genes, and wherein the expression of both portions yields a polyketide.
52. The host cell of claim 51 wherein the portions are from the same polyketide gene and wherein the portion on the host cell genome is different than the portion that is on the plasmid.
53. The host cell of claim 52 wherein the portions together comprise the entire gene.
54. The host cell of claim 53 wherein the gene is the *pikA* gene cluster.
55. A polyketide produced by the host cell of claim 51.
56. Use of a product of claim 9, 21 or 46 for the manufacture of a medicament for the treatment of a pathological condition or symptom in a mammal.
57. The host cell of claim 7 wherein the nucleic acid sequence encoding DesR is disrupted.

58. A product produced by the host cell of claim 57.
59. The host cell of claim 7 wherein the nucleic acid sequence encoding DesI is disrupted.
60. A product produced by the host cell of claim 59.

0998384-11901  
TOTT "4888660